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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/050,289 | 01/16/2002 | David E. Nichols | 3220-69768 | 7025 |

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| EXAMINER | |
|---|---|
| KIM, JENNIFER M | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1617 | |

DATE MAILED: 07/15/2003

6

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/050,289 | NICHOLS ET AL. | |
| | Examiner | Art Unit | |
| | Jennifer Kim | 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *30 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3,4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

Applicants' election without traverse of claims drawn to a method of treatment of Parkinson's disease in Paper No.5 is acknowledged. The amendment filed April 30, 2003 have been received and entered into the application.

### *Claim Rejections - 35 USC § 112*

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method of treating Parkinson's disease comprising the steps set forth in claim 1 comprising administering "dinapsoline", does not reasonably provide enablement for the term "$D_1$ agonist". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

3. Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, predictability of the prior art, state of the prior art and the

amount of experimentation necessary. All of the **Wands factors** have been considered with regard to the instant claims, with the most relevant factors discussed below.

***Nature of the Invention***: All of the rejected claims are drawn to a method of treating a patient with Parkinson's disease, comprising the steps of administering to the patient a full $D_1$ agonist wherein said agonist has a half-life of less than 6 hours and wherein said agonist is administered periodically at a dose resulting in a first tissue concentration of agonist capable of activating $D_1$ dopamine receptors to produce a therapeutic effect; and reducing said agonist dose at least once every 24 hours to obtain a second lower tissue concentration of agonist wherein said second concentration of agonist results in suboptimal activation of $D_1$ dopamine receptors for a period of time sufficient to prevent induction of tolerance. The nature of the invention is extremely complex in that it encompasses the actual treatment of Parkinson's disease comprising the reducing $D_1$ agonist dose in suboptimal activation of $D_1$ dopamine receptors for a period of time sufficient to prevent induction of tolerance.

***Breath of the Claims:*** The complex of nature of the claims

greatly exacerbated by breath of the claims. The claims encompass treating a patient with Parkinson's disease, which has potentially many different causes (i.e. many different neuronal degradation or combination of degradations). Each of which may or may not be addressed by the administration of the claimed $D_1$ agonist with the method steps comprising suboptimal activation of $D_1$ dopamine receptors for a period of time sufficient to prevent induction of tolerance.

***Guidance of the Specification:*** The guidance given by the specification as to how one would administered the claimed compounds to a subject in order to actually treat Parkinson's disease is minimal. All of the guidance provided by the specification is directed towards treatment with dinapsoline rather than any $D_1$ dopamine agonist.

***Working Examples:*** All of the working examples provided by the specification are directed toward the treatment of Parkinson's disease with dinapsoline comprising suboptimal activation of $D_1$ dopamine receptors for a period of time sufficient to prevent induction of tolerance rather than any $D_1$ agonist.

***State of the Art:*** While the state of the art is relatively high with regard to treatment of Parkinson's disease with a $D_1$ agonist with continual administration with optimal activation of $D_1$ receptors, the state of the art with regard to the concentration of agonist results in suboptimal activation of $D_1$ receptors is underdeveloped. In particular, there do not appear to be any examples or teachings in the prior art wherein a compound similar to the claimed compounds was administered to a subject to result in suboptimal activation of D1 receptors.

***Predictability of the Art:*** The lack of significant guidance from the specification or prior art with regard to the actual treatment of Parkinson's disease comprising administering any $D_1$ agonist results in suboptimal activation with the claimed any $D_1$ agonist makes practicing the claimed invention unpredictable in terms of actual treatment of Parkinson's disease with suboptimal activation.

***The amount of Experimentation Necessary:*** In order to practice claimed invention, one of skilled in the art would have to first envision a combination of appropriate

pharmaceutical carrier, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system for one of the claimed compounds and test the combination in the model system to determine whether or not the combination is effective for treating Parkinson's disease comprising suboptimal activation of $D_1$ dopamine receptors for a period of time sufficient to prevent induction of tolerance. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regard to the treatment of Parkinson's disease comprising administering any $D_1$ agonist resulting suboptimal activation of $D_1$ dopamine receptors for a period of time sufficient to prevent induction of tolerance with any $D_1$ compound, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above, and test the system again. If again unsuccessful, which is likely given the lack of significant guidance form the specification of prior art regarding the treatment of Parkinson's disease comprising administration of $D_1$ agonist result in suboptimal activation of $D_1$ dopamine receptors for a period of time sufficient to prevent induction of tolerance, the entire, unpredictable process would have to be repeated until successful. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention comprising suboptimal activation of $D_1$ dopamine receptors for a period of time sufficient to prevent induction of tolerance in a subject by administration of any $D_1$ agonist.

Therefore, a method of treating Parkinson's disease in a subject comprising administering any $D_{1\ agonist}$ resulting suboptimal activation of $D_1$ dopamine receptors for a period of time sufficient to prevent induction of tolerance is not considered to be enabled by the instant specification.

None of the claims are allowed.

***Allowable Subject Matter***

It is suggested to drawn claims to specific $D_1$ agonist supported by the data in the specification to advance the prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 703-308-2232. The examiner can normally be reached on Monday through Friday 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 703-305-1877. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Theodore J. Criares
Primary Examiner
Art Unit 1617

jmk
July 14, 2003